Docket No.3657-1025
PATENT
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IN THE U.S. PATENT AND TRADEMARK OFFICE

In re application of

Enok TJOTTA Conf. 5328

Application No. 10/530,488 Group 1642

Filed April 6, 2005 Examiner Peter J Reddig

METHOD FOR SELECTION OF COMPOUNDS WHICH INHIBIT CLONAL CELL GROWTH AND USE THEREOF

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Assistant Commissioner for Patents March 17, 2009
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

A Notice of Appeal and a Petition to Withdraw Finality are concurrently filed.

The review is requested for the reasons advanced on the attached sheets:

Respectfully submitted,

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REASONS IN SUPPORT OF REQUEST FOR REVIEW

There has been clear errors in both the rejection and procedure by the Office in this application. First, turning to the prosecution history, on September 17, 2008 an Office Action was mailed which objected to the drawings, rejected claims under 35 USC §112, second paragraph, rejected claims under 35 USC §112, first paragraph, rejected claims under 35 USC §102(b) as being anticipated by PRECHEL et al. (Cancer Letters) evidence by CAR et al. (Toxicological Pathology), rejected a claim under 35 USC §103(a) as being unpatentable over PRECHEL et al., DE ASUA et al. (Proc. Natl. Acad. Sci.) and KAMEI (Cell Biol. Int. Rep.) and rejected a claim under PRECHEL et al. in view of TAMI et al. (USP 4,744,985). This Office Action was made final.

An Amendment was filed on December 17, 2009, which presented amendments and remarks.

An Advisory Action was issued on March 12, 2009 (5 days before the end of the 6 month statutory period) refusing to enter the Amendment. This Advisory Action contained more than four and one half pages of commentary supporting the Examiner's position.

However, this Office Action of September 17, 2008 was necessarily non-final because the applied art references were first cited in this Office Action and there had previously been no art-based rejections of the claims. There has thus been a failure to develop a clear issue between the Applicant and the Examiner, as is set forth in MPEP 706.07.

Also, the Examiner issued the Advisory Action less than a week short of the 6 month statutory date in response to an amendment timely filed 3 months after the issuance of the Office Action. As is set forth in MPEP 706.07(f): "*Replies after final should be processed and considered promptly by all Office personnel.*" Although the Applicant is cognizant of the work load placed on Examiners, the delay in issuance of Advisory Action did not leave the Applicant (who is in Norway) sufficient time to consider the options for response.

The Application should thus be considered as under non-final rejection for both procedural and equitable reasons. Also, a petition to withdraw finality is being concurrently filed.

Independent claim 28 of the present invention should thus be that set forth in the Amendment filed December 17, 2008:

> *28. A method for testing and selecting an agent to determine whether said agent inhibits or stimulates clonal growth, comprising the steps:*
> *a) testing said agent with an in vitro clonal test to study the effect of said agent on cloning, the in vitro clonal step a) comprising:*
> *i) seeding of cells in a suitable medium with or without growth factor,*
> *ii) incubating said cells in suitable temperature and atmosphere with said agent; and*
> *iii) determining the effect of said agent on cloning of said cells;*
> *b) testing the effect that different degrees of local collocation of cells has on the effect of said agent on cloning, the testing the effect step b) comprising:*
> *i) transplanting a tumor cell to an animal, or seeding experimental cell cultures with any of the mentioned cells;*
> *ii) treating the animal with said tumor cell or the cells in experimental cell cultures with said agent;*
> *iii) determining the effect of said agent on cloning of said tumor cell in the animal or of the cells in experimental cell cultures;*

c) testing said agent with an in vivo metastasizing test that determines the effect of said agent on metastasizing cells, the testing said agent step c) comprising:

i) injecting tumor cells in an animal to develop metastases, ascites or local tumors;

ii) applying the agent; and

iii) determining the effect of said agent to affect the liberation of cells, migration, and the ability to form a local tumor;

d) testing said agent with an in vivo test of clonal growth of immune cells stimulated by immunization;

e) evaluating the results obtained with steps a), b), c) and d); and

f) determining and selecting said agent.

The Official Action of September 17, 2008 asserted that the claims are indefinite under 35 USC §112, second paragraph, for omitting certain steps. However, this consideration, as well as better defining terms, was addressed in the Amendment filed December 17, 2008, which should be entered. Also, the Amendment filed December 17, 2008 amended claims to sufficiently to address written description issues raised under 35 USC §112, first paragraph.

Turning to the applied art, PRECHEL et al. evaluated the effects of IL-12 on immune parameters and tumor progression in an animal tumor model in which tumor production of GM-CSF leads to myelopoietic stimulation giving rise to an increased number of immune suppressive GM- progenitor cells that suppress anti-tumor immune responses. However, in PRECHEL et al., there is no effect of IL-12 on metastases, and does not describe a specific affection of clonal growth that is different for collocated and scattered identical cells.

In contrast, the immune modulating effect of the specific clonal inhibitors of the present invention is a side-effect that is not wanted in connection with treatment of tumors or viral infections and is probably significant only for primary immune reactions. Therefore, PRECHEL et al. fail to consider specific clonal inhibitors or enhancers, and IL-12 has no effect on formation of metastases.

CAR et al. is used as evidence of IL-12 is a heterodimeric cytokine produced by several types of cells but also has toxic effects. However, CAR et al. conclude that recombinant murine interleukin (IL) 12 (rmIL-12) exhibits antitumor, antiviral, and antimicrobial activities and can modify allergic inflammatory reactions in animal models. But the specific clonal inhibitors, however, do not have general anti-tumor, antiviral, antimicrobial activities. Treatment with specific clonal inhibitors is expected only to inhibit activity in identical cells that were sparsely seeded in cultures or sparsely distributed among other cells in the body, and CAR et al. do not describe an activity of lL-12 and related substances that are confined to only scarcely distributed identical.

Therefore, the conclusion must be the same for both PRECHEL et al. and CAR et al.

The DE ASUA et al. reference shows that BHK 21/13 fibroblasts grown in the presence of insulin show some characteristics of a transformed strain. The effect is shown both in agar and when grown on surface. But in the present

invention insulin induces growth of normal cells in soft agar medium. Then specific clonal inhibitors can inhibit these cells, but only when they were sparsely distributed in the culture. This is possible since insulin stimulates both collocated cells and sparsely seeded cells in culture. Thus PRECHEL et al. and CAR et al., and DE ASUA et al. fail to consider specific clonal inhibitors or enhancers.

KAMEI does not teach "testing the effect those different degrees of local collocation of cells has on the effect of said agent on cloning," as is set forth in amended claim 28 presented on December 17, 2008.

The effects of the extracts of Tamai et al. are not thus in accordance with the effects of specific clonal inhibitors or stimulators detected by the method of the present invention.

Therefore, the rejections over PRECHEL et al. and the secondary references constitute clear error. Withdrawal of the rejections as being clearly deficient is accordingly respectfully solicited.